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ANAEMIA

Pernicious and General

2nd Edition.

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ANAEMIA

Pernicious and General

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[Ca. 1928]

ANAEMIA

Pernicious and General

INTRODUCTION.

ONE of the most important factors in determining individual well-being is the possession of a normal healthy blood circulation, which has to serve the dual purpose of transporting nourishment from the alimentary tract to all parts of the organism, and also at the same time of conveying an adequate amount of oxygen for the maintenance of metabolic processes throughout the entire system. The blood may also be regarded as a chemical arena in which a continuous battle against opposing forces—infectious and toxic—has to be fought and won. In performing these, amongst other functions, the cells of the blood are being constantly destroyed and eliminated from the circulation. The loss is made good by a continuous production of blood cells within the bone marrow, whence they are transmitted to the blood stream. The normal number of red blood cells in health varies between 5 and 6 million per cubic millimetre of blood. Should the number fall below this level from any cause, anaemia is the result.

Anaemia in general is defined as a deficiency in the number of red blood corpuscles—or of haemoglobin stored within these cells. It is usual to classify the diseases presenting this symptom broadly into two groups, viz.: primary and secondary anaemia. The

former—sometimes termed Idiopathic Anaemia—is the direct result of a lesion in the blood or in the blood-forming organs, whereas in secondary or symptomatic anaemias the lack of blood is due to some other recognisable cause, as for example, haemorrhage, cancer, poisonous substances, etc.

For the diagnosis of anaemia in its several forms an examination of the blood—or the blood count as it is called—is of the greatest value. It is usual to determine the number of red blood corpuscles, the percentage of haemoglobin and the colour index, whilst the blood is also carefully examined for the presence of abnormal corpuscular forms. The blood count of a normal individual falls within the following limits :—

Number of red cells ... 4,500,000 to 5,200,000.
Percentage of Haemoglobin ... 90-102.
Colour index ... ... 1.0.

The haemoglobin percentage is of prime importance, indicating the presence or absence of anaemia. "Some degree of anaemia demanding treatment may be regarded as being present when the haemoglobin percentage is found to be 60 per cent. or below; when 35 per cent is reached the anaemia may be regarded as severe, and when it falls to 20 per cent. or below, the infusion of blood is strongly indicated." (Dyke).

The colour index, which expresses the ratio of haemoglobin to the number of red cells in the blood, is also of value for diagnostic purposes. A low colour index is characteristic of chlorosis and most forms of secondary anaemia, whether the result of disease or haemorrhage. On the other hand a high colour index is characteristic of pernicious anaemia.

PERNICIOUS ANAEMIA.

Pernicious Anaemia, sometimes termed Addison's Anaemia, is a primary anaemia the exact cause of which is at present unknown. Recent investigations, however, tend to show that the disease is the result of faulty development of red cells in the bone marrow, in consequence, perhaps, of a deficiency of some specific substance essential for normal blood formation, although a theory that has many adherents suggests that intestinal infection resulting in the formation of toxins, which the liver fails to eliminate, is the cause of the disease.

Pernicious Anaemia is recognisable by a series of characteristic changes in the blood and the digestive and nervous systems of the patient. The most obvious fact is the paucity of red blood cells in the general circulation. In normal health the blood, as already indicated, usually contains five millions of erythrocytes per cubic millimetre, but in cases of pernicious anaemia this is considerably reduced and the degree and seriousness of the disease can be determined by the extent of the reduction. The lowest red blood count on record appears to be 146,000, whilst counts of 500,000 are by no means uncommon. Counts below 2,000,000 indicate a serious condition of the patient.

The disease was first closely studied by Addison in 1849, who described the symptoms as follows:—

> "It occurs in both sexes, generally, but not exclusively, beyond the middle period of life,

and so far as I know at present chiefly in persons of a somewhat large and bulky frame, and with a strikingly marked tendency to the formation of fat.

It makes its approach in so slow and insiduous a manner that the patient can hardly fix a date to his earliest feeling of that langour which is shortly to become so extreme.

The countenance gets pale, the whites of the eyes become pearly, the general frame flabby rather than wasted; the pulse perhaps large, but remarkably soft and compressible, and occasionally with a slight jerk, especially under the slightest excitement. There is an increasing indisposition to exertion with an uncomfortable feeling of faintness or breathlessness on attempting it; the heart is readily made to palpitate; the whole surface of the body presents a blanched, smooth and waxy appearance; the lips, gums and tongue seem bloodless, the flabbiness of the solids increases; the appetite fails; extreme languor and faintness supervene, breathlessness and palpitation being produced by the most trifling exertion or emotion: some slight oedema is probably perceived about the ankles. The debility becomes extreme: the patient can no longer rise from his bed; the mind occasionally wanders; he falls into a prostrate and half-torpid state, and at length expires. Nevertheless, to the very last, and after a sickness of perhaps several months' duration, the bulkiness of the general frame and the obesity often present a most striking contrast to the failure and exhaustion observable in every other respect."

Diagnosis.

The recognition and diagnosis of pernicious anaemia when fully developed presents no difficulty. It is, however, important to diagnose the disease in its earliest stages, since early treatment increases considerably the prospects of a permanent cure.

A recent authority (Cornell, 1928) in discussing the early diagnosis of pernicious anaemia says :—"The great majority of the patients first consult the physician for weakness. The next largest group complain either of numbness or tingling in the extremities. A smaller group come on account of dyspeptic symptoms. Other more unusual complaints have been noted such as girdle pains, arthralgia, failing vision, dizziness, lack of mental concentration, and intestinal haemorrhage. Most patients exhibit a lemon or grape-fruit tinted pallor, whilst a small group are definitely jaundiced."

One objective sign which is of the greatest importance is deficiency of hydrochloric acid in the gastric secretion (achlorhydria), since in all cases of pernicious anaemia achlorhydria is the rule, although the converse does not hold good. It is estimated that one out of every ten cases of achlorhydria will ultimately develop into pernicious anaemia. Patients who show signs of achlorhydria and complain of numbness and tingling of the extremities or inflammation of the tongue (glossitis) may be regarded as potential cases of pernicious anaemia. In such a case an examination of the blood should be made. In pernicious anaemia the red blood cells are very irregular in size and shape, and the characteristic abnormalities in the microscopical appearance of the blood cells would confirm the diagnosis of an early case of the disease.

The most important diagnostic points in the recognition of early pernicious anaemia may be enumerated as follows :—

1. The blood contains large numbers of greatly enlarged red blood corpuscles (macrocytes, megalocytes and megaloblasts) showing also considerable variations in size and shape (anisocytosis).
2. The red blood corpuscles are markedly diminished in number.
3. The colour index of the blood is high.
4. Bilirubin appears in the blood stream.
5. The number of blood platelets is below normal.
6. The presence of achlorhydria.

Treatment.

Pernicious Anaemia was, until quite recently, regarded as a disease from which there was little or no prospect of recovery, and treatment resolved itself into the exhibition of one or other of the pharmaceutical preparations of arsenic and attention to general hygiene, but so hopeless was the prognosis that the average expectation of life was computed at about $2\frac{1}{2}$ years from the appearance of the first symptom.

During the last few years the dietetic treatment of pernicious anaemia with liver has, however, entirely

altered the picture. It is now generally recognised by medical authorities in every quarter of the globe that the best treatment available for this disease is the inclusion of large quantities of liver in the diet of the patient. The effects of this treatment are at once manifested by a most noteworthy improvement in the patient. Thus quoting from *The Lancet*:—"There now exists an equal unanimity that in liver we possess a remedy which will rapidly restore to normal the blood picture of the patient with pernicious anaemia, although how long the improvement will be maintained and whether or not patients will continuously respond to it is not yet known. The indications at present appear to be that the blood count will remain normal so long as liver is taken."

The *British Medical Journal* also states:—"There is general agreement that, putting it at its lowest, the liver treatment produces effects incomparably better than any previous method . . . The results appear to be equally good whether the liver is given in the fresh form or as an extract."

The improvement which follows liver treatment in cases of pernicious anaemia can be quantitatively determined by observations on the changes which take place in the blood count, particularly the number of red blood corpuscles and the percentage of haemoglobin. With an adequate dosage of liver the erythrocyte count may be expected to rise to the normal five millions in the course of two to three months.

The reticulocyte count is also particularly useful for determining at an early stage whether the case will

respond to the treatment, for the proportion of reticulocytes rises considerably within three days of commencing the treatment. Ordinarily the number of reticulocytes is not more than 1 per cent. of the red cells, but in cases of pernicious anaemia under liver treatment the number often increases to 30 per cent. within a week. Subsequently there is a steady and continuous increase in the number of red cells as the number of reticulocytes returns to normal.

"Once the anaemia has completely disappeared the amount of liver that the patient must continue to take varies with the individual; in some patients it may be reduced considerably, whilst in others even a small diminution is followed by deterioration of the blood condition; the only recorded cases of relapse have been in patients who have reduced the liver diet too much or have abandoned it altogether." (Brit. Med. Journ., Dec., 1928).

SECONDARY ANAEMIA.

Secondary Anaemia, resulting from haemorrhage, infection, cancer, poisons, nutritional disturbances or other causes is usually associated with a reduction in the number of red blood cells and in the percentage of haemoglobin.

Robins and Whipple state as a result of their investigations on this subject that "severe experimental (secondary) anaemia produced in animals by bleeding can be cured by a diet of liver, which has an extraordinary effect in producing a maximum regeneration of blood haemoglobin and red cell."—(Robbins and Whipple, *Amer. Jour. Physiol,* 1925).

Consequently liver has also been recommended in the treatment of this form of anaemia, although the clinical data in support of this application of liver treatment are not so complete or so universally accepted as in the case of pernicious anaemia.

The Lancet, discussing this question in a leading article of 28th April, 1928, says:—"Most of the experimental work (of Gibson and Howard on the use of liver, etc., in the cure of anaemia) was performed on animals suffering from secondary anaemia, the result of bleeding. The experiments tend to confirm those of Whipple and his associates, that in experimental anaemia in dogs, blood regeneration is hastened on a diet containing meat, liver and other iron rich foods. *The treatment should then be of use in the secondary anaemias met with in medical practice."*

These conclusions have been recently fully confirmed by clinical results.

THE USE OF "LIVEROID" FOR THE TREATMENT OF ANAEMIAS— GENERAL OR PERNICIOUS.

The treatment of pernicious anaemia as originally recommended by Drs. Minot and Murphy consists in the inclusion of 150-200 grams of liver per day in the diet of the patient. To most patients the daily consumption of such large quantities of liver is very distasteful, and in some cases extremely nauseating, and in consequence we have received many requests from medical practitioners to undertake the manufacture of a *palatable* preparation containing the therapeutic principle of liver in concentrated form though otherwise unaltered. "Liveroid" is the outcome of this demand.

"Liveroid" is a concentrated preparation of the natural uncoagulated juice of liver, and is highly suitable for use in place of liver for the treatment of anaemia *in all its forms.* It offers numerous advantages over cooked liver, as for example :—

1. "Liveroid" is quite pleasant to take, whilst the continuous consumption of liver in the required quantity is distasteful and often nauseating.

2. "Liveroid" is easily administered in the correct dosage and can be given in the form of an appetising beverage.

3. "Liveroid" is manufactured and concentrated by a special process at a low temperature. The therapeutic principles of the liver are thus obtained unimpaired in potency.

The process of manufacture of "Liveroid" is such that the active principles are thoroughly extracted and kept in a state of preservation. In addition the process also extracts the natural liver proteins which have been proved of great importance for the successful treatment of secondary anaemias.

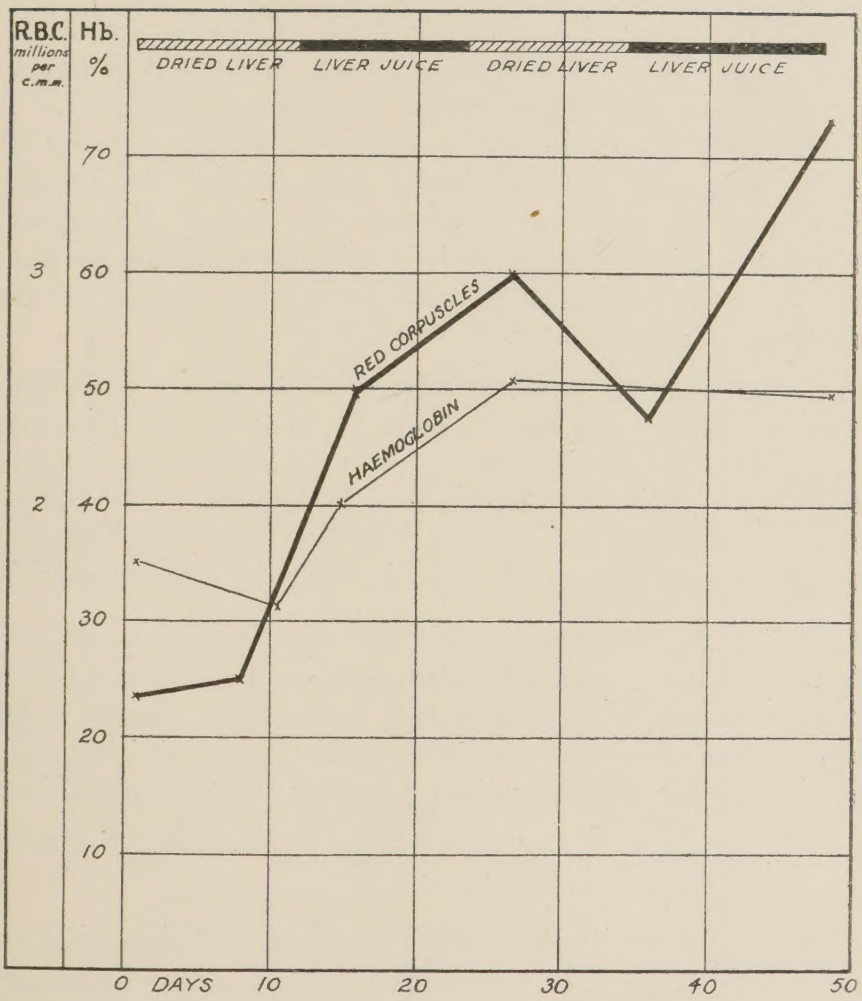
"LIVEROID"—CLINICAL TESTS.

In Pernicious Anaemia.

Clinical trials of "Liveroid" in the treatment of pernicious anaemia have shown that the preparation gives excellent results.

Amongst the recorded cases of this disease treated in the Birmingham General Hospital (A. P. Thompson, *Lancet,* 1928, I, 876), there occurs a woman of 48, who had been anaemic many years, was weak, and appeared to be dying. The red blood count was as low as 730,000, the haemoglobin percentage 17, and the colour index 1.16. She was first given liver for 4 days, when the red blood cell rose to 1,938,000 and the haemoglobin to 25. The treatment was then changed to Oxo Limited's Liver Juice ("Liveroid"). In eight days the red blood count had risen to 2,463,000 and the haemoglobin percentage to 42.

Clinical tests of "Liveroid" have also been conducted at the Wolverhampton General Hospital, with highly satisfactory results (S. C. Dyke, *Lancet,* 1928, I, 877; 1068). In these trials the progress of the patients was controlled quantitatively by determinations of the number of red blood cells and the percentage of reticulocytes and haemoglobin. The results obtained in a case of pernicious anaemia treated alternatively with dried liver and liver juice ("Liveroid") are reproduced in graphic form (page 15).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In Secondary Anaemias and General Debility.

"Liveroid" has been found to be an excellent Liver preparation for the treatment of secondary anaemia. It is generally admitted that a high protein diet is good for patients suffering from secondary anaemia. As "Liveroid" is made by a process which *retains* the easily digested uncoagulated protein of the original liver and in addition contains the active therapeutic principles of the liver, it is a highly suitable preparation for the treatment of both pernicious and secondary anaemia.

A physician writing from a large provincial hospital says: "I have been testing your 'Liveroid' in cases of Secondary Anaemia with very good results. Suitable cases are, however, for various reasons, difficult to come by and I have not yet done enough work to justify publication of my results."

Clinical reports received from physicians in all parts of the country confirm the value of "Liveroid" not only in cases of primary and secondary anaemia, but also in the treatment of *general debility,* as shown by the following extracts from letters we have received.

1. Letter received from a Harley Street Physician :—

"I am just on my last dose of 'Liveroid' and I am glad to say it has kept up, and increased, my red blood cells. I shall certainly prescribe it in all my cases.

"For post operative haemorrhage, in tonsillectomy and in chronic haemorrhoids it is invaluable."

2. An East London Physician reports to us a case of pernicious anaemia in which the patient had to cease work for three years. He was put on raw liver which was subsequently changed for Oxo Limited's "Liveroid." There was a decided improvement on raw liver, but on "Liveroid" the patient progressed rapidly and was so improved that he was able to recommence work.

3. Letter received from patient:—

"I find the Liver Juice not unpleasant to take, *and much to be preferred to cooked liver.*"

A London physician reports that six cases of secondary anaemia treated with "Liveroid" showed marked improvement in all.

A family physician reports that he has had excellent results in the treatment of a growing girl suffering from general debility. Within a week of commencing the treatment the improvement was so marked as to impress the patient's family.

A London physician reports that he prescribed "Liveroid" for his son, who for the last year had been generally anaemic. After the equivalent of 18 ozs. liver had been consumed there was improvement, and after the equivalent of $3\frac{1}{4}$ lbs. his colour had returned and the general tone was much improved.

Dosage.

One part by weight of "Liveroid" is equivalent to 4 parts of fresh liver. Two to three tablespoonfuls (35-50 grams) of the preparation represents approximately the dosage recommended by the pioneers of this treatment.

In cases of secondary and milder forms of anaemia, one tablespoonful of "Liveroid" should be taken per day. "Liveroid" is best taken with a small quantity of warm or tepid water. Hot water should not be used as it causes coagulation of a portion of the highly nutritious proteins contained in the preparation.

Drs. Minot and Murphy's Scheme of Diet in Cases of Pernicious Anaemia.

1. Liver (beef, calves, or chicken) freshly cooked without fat. At least 4 ozs. (110 grams)—preferably 7 ozs. (200 grams) or more, weighed after cooking.

   (Many physicians prefer to prescribe the equivalent quantity of "Liveroid"—2-3 tablespoonfuls per day or alternately half the dosage in the form of cooked liver, and half in the form of "Liveroid.")

2. Fruits—preferably fresh—*especially* peaches, apricots, pineapple, strawberries, oranges and grape-fruit, allowed freely.

3. *Vegetables* containing one to ten per cent. of carbo-hydrates, preferably fresh—cooked or raw. Not less than ten ounces (300 grams), lettuce, spinach, asparagus, cabbage and tomato are especially desirable.

4. *Fats restricted,* not over two and a half ounces (70 grams). Avoid cheese, bacon, fried food. Allow but little cream and butter, and not more than one egg.
   Use mineral oil for salad dressings.

5. Starchy foods, as cereals, potato, bread, add to suit individual desires, but not to the exclusion of the requirements given above.

The starchy foods are best crusty or dextrinated. Whole wheat toast is desirable.

6. Milk is best limited to about eight or nine ounces (240 c.c.).

7. Tea and coffee as desired.

8. Avoid grossly sweet food; yet allow sugar sparingly.

9. Avoid excess of salt.

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